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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/525,986

02/25/2005

Tadashi Nakajima

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EXAMINER

BASQUILL, SEAN M

ART UNIT

PAPER NUMBER

4161

MAIL DATE

DELIVERY MODE

07/29/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/525,986	<b>Applicant(s)</b> NAKAJIMA ET AL.	
	<b>Examiner</b> Sean Basquill	<b>Art Unit</b> 4161	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 30 May 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 5-8, and 17-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 13-16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 25 February 2005 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☒ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>See Continuation Sheet</u> .                                  | 6) <input type="checkbox"/> Other: _____                          |

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :25 Feb 2005; 16 May 2005; 16 Aug 2007; 5 Sep 2007.

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicant's election of a composition of matter, Claims 1-4, and 13-16, in the reply filed on 30 May 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 5-12, and 17-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 30 May 2008.

2.

### ***Priority***

3. Applicants claim to the effective filing date of the PCT Application JP03/1004, filed 29 August 2003, is hereby acknowledged and granted.

4. Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 119(a)-(d) based upon an application filed in Japan on August 29, 2002.

### ***Information Disclosure Statement***

6. The information disclosure statements filed 5 September 2007, 16 August 2007, and 16 May 2005 fail to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language; the documents to which this statement refers have been designated on

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the enclosed IDS by the line-through. It has been placed in the application file, but the information referred to therein has not been considered.

***Objections: Specification***

7. The examiner notes that the specification appears to be a machine translation of the original Japanese language specification. As such, a number of idiomatic idiosyncrasies have been noted, including Page 3, paragraphs 1-4, Page 6 paragraph 2, the second to last sentence of paragraph 1 on page 7, and page 8 paragraph 2, to name a few. A substitute specification in proper idiomatic English and in compliance with 37 CFR 1.52(a) and (b) is required. The substitute specification filed must be accompanied by a statement that it contains no new matter.

***Objections: Drawings***

8. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not defined in the description: Figures 1 and 3 refer to “Compound A,” Figures 2 and 4 refer to “Compound B,” without providing an indication as to the identity of Compounds A and B. Corrected drawing sheets in compliance with 37 CFR 1.121(d), **or** amendment to the specification to define the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either “Replacement Sheet” or “New Sheet” pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and

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informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
  2. Ascertaining the differences between the prior art and the claims at issue.
  3. Resolving the level of ordinary skill in the pertinent art.
  4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
9. Claims 1-4, and 13-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP/0286903A1 (hereinafter “Bito”), in view of U.S. Patent 7,015,210 (hereinafter “Aiken”), P. Vasantha Rao, et al, *Modulation of Aqueous Humor Outflow Facility by the Rho Kinase-Specific Inhibitor Y-27632*, 42 INV. OPHTHALMOL. VIS. SCI. 1029 (April 2001), and U.S. Patent 6,271,224 (hereinafter “Kapin”).
10. Bito indicates that medical treatment of glaucoma commonly requires combination therapy owing to the fact that increased intraocular pressure (IOP) often cannot be controlled by a single therapy. (C.3, L.14-17). Bito continues on to indicate that regulating both the production and outflow of aqueous humor are effective in treating IOP, and further describe the

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two pathways responsible for maintaining the outflow of aqueous humor; through the trabecular meshwork and uveoscleral routes. (C.2, L.37-49). Bito also indicates that prostaglandin derivatives reduce IOP by increasing uveoscleral outflow. (C.1, L.48-50). Bito neither specifically recites any of the claimed prostaglandins, nor specifies rho-kinase inhibitors as effective combination therapeutics.

11. Aiken echoes the Bito insistence on the use of combination therapy including prostaglandins in the treatment of IOP. (C.9, L.66-C.10, L.11) Aiken further indicates that prostaglandins such as latanoprost, unoprostone isopropyl, and travaprost, among others, which are known to treat IOP can also be used as part of combination therapy when paired with a compound or drug which operates through a distinct mechanism of action. (C.10, L.2-7, 19-31). Aiken, like Bito, prefers combination therapies utilizing both an outflow enhancing agent and an aqueous humor production reducing agent, here an epoxy-steroidal aldosterone receptor antagonist (C.10, L.1—26), but emphasizes that complementary mechanisms of action are the primary concern (c.10, L.7-11).

12. Rao indicates that the rho-kinase inhibitor Y-27632 ([(+)-R-trans-4-(1-aminoethyl)-N-(4-pyridyl) cyclohexanecarboxamide] (Rao *at* 1030), appear to improve aqueous outflow through the trabecular meshwork (Schlemm's canal). (*Id.* *at* 1034).

13. Kapin indicates isoquinoline compounds, preferably 1-(5-isoquinolinesulfonyl)-homopiperazine are effective in lowering IOP. (C.2, L.31-33; C.3, L.19-24).

14. Because Bito and Akin both teach that while individual drugs such as prostaglandins may be effective in treating IOP, combination therapy, in particular those therapeutic combinations which effect IOP through distinct mechanisms of action, are preferable modes of treatment, it

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would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine prostaglandins with alternative IOP therapeutics operating by distinct modes of action. Because Bito indicates prostaglandins work by effecting the uveoscleral mode of outflow, and Rao indicates that rho-kinase inhibitors effect outflow through the trabecular meshwork, a distinct mechanism of action in reducing IOP, combining the teaching of Bito and Rao would have been obvious to one of ordinary skill in the art. Likewise, one of ordinary skill in the art, give the teachings of Bito, Akin, and Rao, would have been provided ample motivation to include the teaching of Kapin, because the Rho-kinase inhibitor disclosed in Rao is used to treat the same condition as that disclosed in Kapin.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean Basquill whose telephone number is (571) 270-5862. The examiner can normally be reached on Monday through Thursday, between 8AM and 6PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick Nolan can be reached on (571) 272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SMB

/Patrick J. Nolan/  
Supervisory Patent Examiner, Art Unit 4161